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EXTERNAL PREPARATION FOR SKIN FOR WHITENING

[美白用皮膚外用剤]

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(54) [Title of the Invention] EXTERNAL PREPARATION FOR SKIN FOR WHITENING

(57)Abstract:

PROBLEM TO BE SOLVED: To obtain the subject novel external preparation that has excellent skin-whitening effect with high safety by using an extract from a plant belonging to the genus Croton (family Euphorbia Helioscopia).

SOLUTION: The roots, trunks, branches, leaves, stems containing underground stems, flowers, fruits or the whole plant body of a plant belonging to the genus Croton such as Croton birmanicus or velame do campo folhas (Croton campestris) are extracted with a polar solvent such as

water, a lower alcohol, aqueous alcohol, propylene glycol, 1,3-butylene glycol or butanol or with an organic solvent such as chloroform, dichlorethane, carbon tetrachloride, acetone, ethyl acetate or ether by soaking or refluxing, and the resultant extract solution is filtrated and concentrated to prepare an extract. The objective cosmetic contains the extract in an amount of 0.0005 to 10.0 wt.%, preferably 0.005 to 5.0 wt.% on the dry basis.

[Claims]

[Claim 1] Skin external preparations for whitening characterized by containing the extract of the Euphorbiaceae croton seed (Croton) group plant.

[Claim 2] Skin external preparations for whitening according to claim 1 whose Euphorbiaceae croton seed (Croton) group plant is HASSAKUN (scientific name: Croton birmanicus).

[Claim 3] Skin external preparations for whitening according to claim 1 whose Euphorbiaceae croton seed (Croton) group plant is BERAMEDOKAMPOFORUHASU (velame do campo folhas, scientific name: Croton campestris).

[Claim 4] Skin external preparations for whitening according to claim 1, 2, or 3 whose content of the extract of said Euphorbiaceae croton seed (Croton) group plant is 0.0005 to 10.0 wt.% to the total quantity of skin external preparations.

[Claim 5] A whitening agent characterized by consisting of an extract of the Euphorbiaceae croton seed (Croton) group plant.

[Claim 6] The whitening agent according to claim 5 whose Euphorbiaceae croton seed (Croton) group plant is HASSAKUN (scientific name: Croton birmanicus) or BERAMEDOKAMPOFORUHASU (velame do campo folhas, scientific name: Croton campestris).

[Detailed Description of the Invention]

[0001]

[Field of the Invention] This invention relates to skin external preparations for whitening. In more detail, by blending the extract of the Euphorbiaceae croton seed (Croton) group plant as a whitening agent, the generation of melanin is controlled. The invention is especially related to skin external preparations for whitening that are effective in the prevention and the improvement of pigmentation, stains, freckles, chloasma, etc., after receiving a suntan from exposure to sunlight.

[0002]

[Prior Art] Although there is some lack of understanding about developmental mechanisms such as skin staining, generally the stimulus of ultraviolet rays from daylight causes activation of a hormone and melanin is formed, and it is thought that this carries out abnormal deposits on the skin.

[0003] The melanin as the cause of coloring of the skin was produced by melanin generation granulation (melanosome) in melanocytes (melanocytes) between the epidermis and dermis, and is diffused to a contiguous cell by osmosis.

[0004] The biochemical reaction in this melanocyte is presumed to be the following, that is, thyrosin, which is an essential amino acid, serves as a dopa quinone according to an operation of the enzyme tyrosinase, and the process is like an enzyme in that it changes by nonenzymatic oxidation to black melanin.

[0005] Therefore, it is very important to control the melanin generation to control the tyrosinase that is the first step of the reaction.

[0006]

[Problems to be Solved by the Invention] However, every time the conventional compound with which tyrosinase depressant action is known removes hydroquinone, because manifestation of the effect is very slow, the improvement effect of the chromatosis cannot be fully expected.

[0007] On the other hand, although it is accepted that hydroquinone's effect is temporary, because the skin is sensitive, general use is restricted. Then, although there was an attempt (JP58-154507A) for use as a monoester or alkyl mono-ether, etc., of a higher fatty acid in order to improve sensitivity, the difficulty lies in producing a fully satisfied sensitive effect; but because the ester is decomposed by hydrolase in the living body, its use fully satisfies safety concerns.

[0008] The inventors found that the whitening effect was excellent in view of the above-mentioned point, and having a melanin generation depressant action and tyrosinase inhibitory action were excellent in the extract of the Euphorbiaceae croton seed (Croton) group plant, as a result of inquiring wholeheartedly about the melanin generation depressant effect for various matters with the goal of having a whitening agent with high safety developed, completing this invention.

[0009] This invention aims at having an outstanding whitening effect and offers new high skin external preparations for whitening and with a high degree of safety.

[0010]

[Means for Solving the Problems] That is, the skin external preparations for whitening characterized by this invention containing the extract of the Euphorbiaceae croton seed (Croton) group plant are offered.

[0011] Moreover, this invention offers the aforementioned skin external preparations for said whitening whose Euphorbiaceae croton seed (Croton) group plant is HASSAKUN (scientific name: Croton birmanicus).

[0012] Furthermore, this invention offers the aforementioned skin external preparations for said whitening whose Euphorbiaceae croton seed (Croton) group plant is BERAMEDOKAMPOFORUHASU (velame do campo folhas, scientific name:Croton campestris).

[0013] Moreover, as for this invention, the content of the extract of said Euphorbiaceae croton seed (Croton) group plant offers the aforementioned skin external preparations for whitening, which are 0.0005 to 10.0 wt.% of the skin external preparation entire quantity for whitening.

[0014] Furthermore, the whitening agent characterized by this invention consisting of an extract of the Euphorbiaceae croton seed (Croton) group plant is offered.

[0015] Moreover, this invention offers the aforementioned whitening agent whose Euphorbiaceae croton seed (Croton) group plant is HASSAKUN (scientific name: Croton birmanicus) or BERAMEDOKAMPOFORUHASU (velame do campo folhas, scientific name:Croton campestris).

[0016]

[Embodiment of the Invention] Hereafter, embodiments of this invention are explained in full detail.

[0017] As the Euphorbiaceae croton seed (Croton) group plant is used for this invention, HASSAKUN (scientific name: Croton birmanicus) and BERAMEDOKAMPOFORUHASU (velame do campo folhas, scientific name:Croton campestris) are suitable. Especially HASSAKUN is a plant grown on the plains in Thailand, with grass, etc., and especially BERAMEDOKAMPOFORUHASU is a plant grown on the plateau in Brazil, in swamps, etc.

[0018] The extract used for this invention is filtered, condensed and obtained after immersing or heating the entire plants, such as the root of the above-mentioned plant, a trunk, a branch, a leaf, a stem containing an underground stem, a flower, and fruits, with an extracting solvent. If it is the solvent usually used for an extract as an extracting solvent, there is no special limit; for example, it is independent of organic solvents such as polar solvents, such as water, lower alcohol, water lower alcohol, propylene glycol, 1, 3-butylene glycol, and a butanol, or chloroform, dichloroethane, a carbon tetrachloride, an acetone, ethyl-acetate ester, and the ether, or in combination.

[0019] Although a report of the extract of the plant other than the croton seed (Croton) group of Euphorbiaceae has as its example the invention disclosed in (JP5-345720A), in which a plant besides the Aleurites group was used for whitening cosmetics, the melanin generation depressant action of croton seed (Croton) group plant and the application as a whitening agent are not known at all.

[0020] The loadings of the extract of the Euphorbiaceae croton seed (Croton) group plant in this invention are 0.005 to 5.0 wt.%, preferably 0.0005 to 10.0 wt.%, as dry matter weight among skin external preparations for whitening. Pharmaceutical preparation is difficult when the effect referred to is less than 0.0005 wt.%, and when it exceeds 10.0 wt.%, it is not desirable. Moreover, even if there is blending of 5.0 wt.% or more, a big improvement is not found.

[0021] In the skin external preparations for whitening of this invention, in a range that does not spoil the effect of this invention other than the above-mentioned indispensable components, the whitening agent of others other than the component usually used for skin external preparations, such as cosmetics and drugs, for example, the above-mentioned indispensable component, a moisturizer, an antioxidant, an oily component, an ultraviolet ray absorbent, a surfactant, a thickener, alcohols, a powder component, color material, an aqueous component, water, various skin nutrients, etc., can be blended suitably if needed, and can be manufactured by conventional methods.

[0022] The skin external preparations for whitening of this invention mean the external preparations applied to the skin for the purpose of whitening such as ointment, a cream, a milky lotion, a lotion, a pack, and baths, as cosmetics, drugs, and quasi drugs.

[0023]

[Embodiment] Next, an example explains this invention in further detail. In addition, this invention is not limited only to these embodiments. All loadings are wt.%.

[0024] First, the test method for the melanin depressor effect, the tyrosinase activity inhibition effect, and the whitening effect of an extract of this invention and its results are explained.

[Euphorbiaceae croton seed (Croton) group plant]

[0025] [Test Method and Results]

1. Adjustment of a sample: 100g parts of the trunk of Euphorbiaceae croton seed (Croton) group plant extract HASSAKUN were immersed in ethanol for one week at room temperature, the extract was condensed, and 1.2g of ethanol extracts were obtained. Moreover, BERAMEDOKAMPOFORUHASU was

immersed in ethanol for one week at room temperature in 100g parts of a leaf, condensed to obtain 2.1g of ethanol extracts. Each extract was melted 1% to DMSO, the solution was diluted, concentration was adjusted, and the following experiments were conducted using these.

[0026]2. Cell Culturing Method

B16 melanoma cultured cells of mouse origin were used. It is CO_2 in the MEM culture medium that contains FBS and theophylline (0.09mg/ml) 10%. It was cultivated in an incubator (95% air, 5% carbon dioxide) and under 37°C conditions. Twenty-four hours after culturing, the sample solution was added so that it might become 10^{-2} to 10^{-5} wt.% with final concentration (extract dry matter conversion concentration). The culture was continued for 3 more days, and the amount of melanin generation and the tyrosinase activity inhibition effect were measured by the following methods.

[0027]3. Visual Appreciation Measurement for Melanin Amount

The diffusion plate was placed on the lid of the plate of a well, and the amount of melanin intracellular was observed with an inverted microscope and compared with the case of the sample (criteria), which had not added the extract of the Euphorbiaceae croton seed (Croton) group plant. The results are displayed in Table 1. Moreover, the same trial, also about the Mallotus japonicus (Euphorbiaceae Mallotus japonicus group) extract with which melanin generation depressant action is reported as an embodiment of the above reference, was performed. The results are combined and shown in Table 1.

[0028] < criterion >

O: White (the amount of melanin)

Δ: Slightly white (the amount of melanin).

x: Criteria (the amount of melanin)

[0029] 4. Measurement of tyrosinase activity

Remove the inner culture medium and wash it twice using PBS 100µl.

Each PBS contains 1% Triton-X (Loam under Haas, surfactant) of 45µl in a well and was added. The plate was vibrated for one minute, the cell membrane was often destroyed, the absorbance of 475nm was measured with the microplate reader, and this was made into the absorbance at zero minutes. Then the L-DOPA solution of 10mM(s) of 5microl was added quickly, and it was moved to the 37°C incubator and was made to react for 60 minutes. The plate was vibrated for one minute, and the absorbance (475nm) of 60 minutes was measured. The tyrosinase activity (%) is considered to be the ratio of the degree of light absorption of the material with added plant extract with respect to the light absorption difference at zero minutes and 60 minutes in the case of material (control) that has not added plant extract. The result is shown in Table 1. Moreover, the same trial as the above was also performed for the ethanol extract of Mallotus japonicus (Euphorbiaceae Mallotus japonicus group) as an embodiment, for reference. The results were combined and are shown in Table 1. In addition, in the table "-" means comparing to the control, and a significant difference was not accepted at less than 5% of the level of significance, compared with the control.

[0030]

[Table 1]

Experiment	Melanin general visual appearance evaluation			Tyrosinase activity (%)		
Concentration (wt.%)	10^{-4}	10^{-3}	10^{-2}	10^{-4}	10^{-3}	10^{-2}
HASSAKUN extract	X	X	O	85	82	39
BERAMEDOKAMPOFO extract.	O	O	toxic	79	33	toxic
Mallotus japonicus	X	X	X	-	-	85

[0031] 5. Whitening Effect Test

The cosmetics for whitening with the following formulas were applied for 4 weeks, one unit once every morning and evening for 5 days before exposed to sunlight for 40 test subjects' underarm inside section skin exposed to the sunlight of the summer for 4 hours (a 2-day period, 2 hours per day). A test subject's special panel was divided into 8 groups, considered as 5 groups, and the whitening effect was judged by the following evaluation approaches, and the result was shown in Table 2. In addition, the HASSAKUN and the BERAMEDOKAMPOFORUHASU extracts, which were used for the trial, carry out concentration hardening by drying of the ethanol extract obtained above "1. the adjustment: Euphorbiaceae croton seed (Croton) group plant extract of a sample."

[0032]

[Cosmetics for whitening]

(Alcoholic phase)

95% ethyl alcohol 55.0 wt%

Polyoxyethylene (25 mol) hydrogenated-castor-oil ether 2.0

An antioxidant and antiseptics optimum dose

Perfume optimum dose

Whitening agent in ("Table 2") Amount in "Table 2"

(Aqueous phase)

Glycerol 5.0

Hexametaphosphoric acid sodium optimum dose

Ion exchange water residuals

<Manufacturing Method> An aqueous phase and an alcoholic phase are prepared, respectively, and both are mixed and

dissolved after that.

[0033] [Evaluation Method]

The light-colored effect was judged based on the following criteria.

< criteria >

O: when higher efficacy and the shown effective percentage are 80% or more among test subjects

☼: when higher efficacy and the shown effective percentage are 50% to less than 80% among test subjects

Δ: when higher efficacy and the shown effective percentage are 30% to less than 50% among test subjects

x:: the case where higher efficacy and the shown effective percentage are less than 30% among test subjects [0034]

[Table 2]

Whitening Agent	Loading (wt. %)	Whitening Effect
No additive	-	x
hydroquinone	1.0	Δ
HASSAKUN	0.1	O
HASSAKUN	1.0	O
HASSAKUN	10.0	☼
BERAMEDOKAMPOFORUHASU	0.1	O
BERAMEDOKAMPOFORUHASU	1.0	O
BERAMEDOKAMPOFORUHASU	10.0	☼

[0035] Tables 1 and 2 show that the Euphorbiaceae croton seed (Croton) group plant extract has outstanding melanin depressant action, tyrosinase activity depressant action, and whitening effect. Below, the embodiment of other skin external preparations for whitening with this invention is shown.

[0036]

"Embodiment 1 Cream"

(Formula)

Stearic acid 5.0 wt.%
Stearyl alcohol 4.0
Isopropyl myristate 18.0
Glycerol monostearin acid ester 3.0
Propylene glycol 10.0
HASSAKUN methanol extract 0.01
Caustic potash 0.2
Sodium hydrogensulfite 0.01
Antiseptics Optimum dose
Perfume optimum dose
Ion exchange water

Propylene glycol, a HASSAKUN methanol extract, and caustic potash are added in residual (process) ion exchange water and dissolved, and the mixture is heated and kept at 70°C (aqueous phase). Other components are mixed, and heating fusion is carried out at 70°C (oil phase). Because an oil phase is added gradually, and it all finishes by adding it to the aqueous phase, it maintains the temperature for a while, and a reaction is caused to be made. Then the mixture is cooled to 30°C, emulsifying to homogeneity and stirred well by a homomixer.

[0037]

"Embodiment 2 cream"

(Formula)

Stearic acid 2.0 wt.%

Stearyl alcohol 7.0

Hydrogenation lanolin 2.0

Squalane 5.0

2-octyldodecyl alcohol 6.0

Polyoxyethylene (25 mols)

cetyl alcohol ether 3.0

Glycerol monostearin acid ester 2.0

Propylene glycol 5.0

HASSAKUN ethanol extract 0.05

Sodium hydrogensulfite 0.03

Ethylparaben 0.3

Perfume optimum dose

Ion exchange water

Propylene glycol is added and heated to a residual (process) with ion exchange water and kept at 70°C (aqueous phase). Other components are mixed, heating fusion is carried out, and the mixture is kept at 70°C (oil phase). After an oil phase is added to the aqueous phase, performing preliminary emulsification and emulsifying to homogeneity by the homomixer, the mixture is cooled to 30°C and stirred well.

[0038]

"Embodiment 3 cream"

(Formula)

Solid paraffin	5.0 wt.%
Yellow beeswax	10.0
Vaseline	15.0
Liquid paraffin	41.0
Glycerol monostearin acid ester	2.0
Polyoxyethylene (20 mols) sorbitan Mono-lauric-acid ester	2.0
Soap powder	0.1
PARAMETOKISHI cinnamic acid 2-ethylhexyl	1.5
Borax	0.2
HASSAKUN acetone extract	0.05
BERAMEDOKAMPOFORUHASU ethanol extract	0.05
Sodium hydrogensulfite	0.03

Ethylparaben 0.3

Perfume optimum dose

Ion exchange water soap powder and borax are added to residual (process) ion exchange water, heating dissolution is carried out, and the mixture is kept at 70°C (aqueous phase). Other components are mixed, heating fusion is carried out, and the mixture is kept at 70°C (oil phase). In addition, it reacts gradually, stirring an oil phase to the aqueous phase. It is cooled to 30°C after reaction termination, emulsifying to homogeneity and stirring with sufficient emulsification back by the homomixer.

[0039]

"Embodiment 4 Milky Lotion"

(Formula)

Stearic acid 2.5 wt.%

cetyl alcohol 1.5

Vaseline 5.0

Liquid paraffin 10.0

Polyoxyethylene (ten mols)

mono-oleate 2.0

Polyethylene glycol 1500

3.0 Triethanolamine

1.0 Carboxyvinyl polymer 0.05 (trade name: Carbopol 941 and B. F. Goodrich Chemical Company)

A HASSAKUN ethanol extract 0.01

BERAMEDOKAMPOFORUHASU ethyl-acetate ester extract 0.03

Sodium hydrogensulfite 0.01

Ethylparaben 0.3

Perfume optimum dose ion exchange water A carboxyvinyl polymer is dissolved in the ion exchange water of residual (process) small quantity (A phase). Polyethylene glycol 1500 and triethanolamine are added to the remaining ion exchange water, the heating dissolution is carried out, and the mixture is kept at 70°C (aqueous phase). Other components are mixed, heating fusion is carried out, and the mixture is kept at 70°C (oil phase). An oil phase is added to the aqueous phase, preliminary emulsification is performed and an A phase is added, and it is cooled to 30°C, carrying out homogeneity emulsification and stirring with sufficient emulsification by the homomixer.

[0040]

"Embodiment 5 Milky Lotion"

(Formula)

A micro crystallin wax 1.0 wt.%

density low 2.0

Lanolin 20.0

Liquid paraffin 10.0

Squalane 5.0

Sorbitan sesquioleate 4.0

Polyoxyethylene (20 mols)

sorbitan Mono-oleate 1.0

Propylene glycol 7.0

BERAMEDOKAMPOFORUHASU ethanol extract 5.0

Sodium hydrogensulfite 0.01

Ethylparaben 0.3

Perfume optimum dose

Ion exchange water propylene glycol is added and heated to residual (process) ion exchange water, and the mixture is kept at 70°C (aqueous phase). Other components are mixed, heating fusion is carried out, and the result is kept at 70°C (oil phase). The aqueous phase is gradually added to this, stirring in an oil phase, and it is emulsified to homogeneity by the homomixer. It is cooled to 30°C, stirring with sufficient emulsification.

[0041]

"Embodiment 6 Jelly"

(Formula)

95% Ethyl alcohol 10.0 wt.%

dipropylene glycol 15.0

Polyoxyethylene (50 mols)

Oleyl The alcoholic ether 2.0

Carboxyvinyl polymer 1.0

(trade name: Carbopol 940

and B. F. Goodrich Chemical Company)

Caustic alkali of sodium 0.15

L-arginine 0.1

HASSAKUN ethanol extract 7.0

2-hydroxy - 4 - Methoxybenzophenone Sulfonic-acid sodium 0.05 Ethylenediamine tetra-acetate, 3 sodium, and 2 water 0.05

Methylparaben 0.2

Perfume optimum dose

Ion exchange water Carbopol 940 is dissolved in residual (process) ion exchange water at homogeneity, and on the other hand, 50% ethanol water-solution extract of brown-eared bulbul funnels and the polyoxyethylene (50 mols) oleyl alcohol ether are dissolved in ethanol 95%, and added to the aqueous phase. Subsequently, after other components are added, it is made to neutralize by caustic alkali of sodium and L-arginine, and thickens.

[0042]

"Embodiment 7 Essence"

(Formula)

(A phase)

95% Ethyl alcohol 10.0 wt.%

polyoxyethylene (20 mols)

octyl dodecanol 1.0 Pantothenyl ethyl ether 0.1

HASSAKUN methanol extract 1.5

BERAMEDOKAMPOFORUHASU methanol extract 0.1

Ascorbic-acid glucoside 1.5

Arbutin 3.0

Methylparaben 0.15

(B phase)

Potassium hydroxide 0.1

(C phase)

Glycerol 5.0

Dipropylene glycol 10.0

Sodium hydrogensulfite 0.03

Carboxyvinyl polymer 0.2 (trade name: Carbopol 940 and B. F. Goodrich Chemical Company)

Purified water A residual

(Process)

An A phase and a C phase are dissolved in homogeneity, respectively, and an A phase is added and dissolved to the C phase. Subsequently, restoration is performed after adding a B phase.

[0043]

"Embodiment 8 Pack"

(Formula)

(A phase)

Dipropylene glycol 5.0 wt.%

polyoxyethylene (60 mols)

hydrogenated castor oil 5.0

(B phase)

A HASSAKUN methanol extract 0.01

olive oil 5.0

tocopherol acetate 0.2

ethylparabens 0.2

perfume 0.2

(C phase)

A sodium hydrogensulfite 0.03

polyvinyl alcohol 13.0 (90 whenever [saponification] polymerization degree 2,000)

Ethanol 7.0

purified water A residual

(Process)

An A phase, a B phase, and a C phase are dissolved in homogeneity, respectively, and a B phase is added and dissolved to an A phase. Subsequently, restoration is performed after adding this to the C phase.

[0044]

"Embodiment 9 Cake Makeup"

(Formula)

Talc 43.1 wt.%

kaolin 15.0

sericites 10.0

zinc whites 7.0

titanium dioxides 3.8

Synthetic Ochre 2.9

black iron oxide 0.2

squalane 8.0

isostearic acid 4.0

mono-oleic acid POE sorbitan 3.0

octanoic-acid isocetyl 2.0

HASSAKUN ethanol extract 1.0

antiseptics optimum dose

perfume

The powder component of optimum dose

(Process)

talc - black iron oxide is sufficiently mixed with a blender, and after adding the oily component of squalane - octanoic-acid isocetyl, a HASSAKUN ethanol extract, antiseptics, and perfume and kneading them, the result is cast in a container.

[0045]

[Embodiment 10 emulsification mold foundation (cream type)]

(Formula)

(Fine-particles section)

A titanium dioxide 10.3 wt.%

sericite 5.4

kaolins 3.0

Synthetic ochre 0.8

red ochre 0.3

black iron oxide 0.2

(Oil phase)

Decamethyl cyclopentasiloxane 11.5

liquid paraffins 4.5

Polyoxyethylene denaturation dimethylpolysiloxane 4.0

(Aqueous phase)

Purified water 50.0

1, 3-butylene glycol A 4.5

HASSAKUN ethanol extract 1.5

sorbitan sesquioleate 3.0

antiseptics optimum dose

perfume

The fine-particles section that fully carried out preferential grinding of the optimum dose

(Process) After heating, the aqueous phase churning is added, and homomixer processing is carried out. Furthermore, after adding the oil phase carrying out heating, mixing and homomixer processing, and agitating, perfume is added and the mixture is cooled to a room temperature.

[0046]

[Effect of the Invention] According to this invention, while having outstanding melanin generation depressant action and tyrosinase activity inhibitory action and having an effect excellent in light-coloring of the pigmentation, the stain, freckle, chloasma, etc., after sun tanning, and whitening, the skin externally, there can be preparations made for whitening, and a whitening agent excellent also for safety can be offered.